REMARKS

1. It is noted with appreciation that the objection to the specification has been overcome by the previous amendment.

2. Claims 1-3 and 6-11 were rejected under 35 U.S.C. §102(b) in view of Tay et al. (Biomaterials, 1989, vol. 10(1), pp.1-15) or Larsson et al. (WO 93/05793). Applicants respectfully traverse this rejection for the following reasons.

A central issue that is in dispute is whether Tay discloses a carbohydrate chain W in each monomeric unit as claimed by Applicants. Applicants do not believe that Tay's use of tresyl chloride activates the OH groups in every monomer in the activation step. There would be unreacted OH groups on the PVA that would not bind to heparin. Thus, Tay does not disclose polymer with heparin attached to every repeating unit.

The Office Action has resorted to Nilsson et al. (Biochemical and Biophysical Research Communication, 1981, 102(1), 449-457) in an attempt to supplement the disclosure of Tay on this issue. Because references may not be combined in a §102 rejection, it is assumed that the Office Action is asserting that Nilsson forms a part of Tay's disclosure.

The Office Action points out that Nilsson discloses that the activation of OH groups with tresyl chloride occurred at a "high amount" (>1 mmol/g dry product) after 10 minutes of reaction. The Office Action asserts that Tay uses the same process as Nilsson and thus, that the OH groups in every repeat unit in Tay would be activated and would be bound to heparin.

More specifically, Applicants submit that Tay, using the same process as Nilsson, does not activate all OH groups with tresyl chloride and thus, fails to produce a polymer with a carbohydrate group W in each repeating unit as claimed. Nilsson activates OH groups on sepharose, which is constituted by agarose. Agarose has the following composition: D-galactose + 3,6-anhydro-L-galactose (molecular weight of the

repeating unit being 342). D-galactose contains OH groups, but 3,6-anhydro-L-galactose does not. There are 2.92 milli-mols of OH per gram of sepharose. Table 1 of Nilsson shows that the highest level of tresyl groups formed on the sepharose support was 1.35 milli-mols per gram (mmol/g). Although the Office Action appears to characterize this as a "high amount" this only represents binding of 46% of the available OH groups in 1 gram of sepharose. This means that Nilsson believed that achieving activity of more than 50% of the OH groups would be difficult. Thus, Nilsson does not disclose activation of all OH groups and Tay's use of the same technique does not disclose activation of all OH groups or binding of heparin to every repeat unit.

Rejections under §102 leave no room for speculation and require disclosure of all elements of the claimed invention either expressly or inherently. For there to be inherent anticipation, it must be clear that the features of the invention are consistently met each time when following the disclosure of the reference. There can be no experimentation, approximation or guesswork involved. "Inherent anticipation requires that the missing descriptive material is 'necessarily present,' not merely probably or possibly present, in the prior art." Trintec Indust., Inc. v. TOP-USA Corp., 63 USPQ2d 1597 (Fed. Cir. 2002), citing Continental Can Co. USA, Inc. v. Monsanto Co., 20 USQD2d 1746 (Fed. Cir. 1991). It is respectfully submitted that the Office Action is speculating that the claimed features are met. Applicants have shown that it is unlikely that Tay could achieve the features of the claimed invention, let alone do so consistently.

In general, chemical reactions involving a polymer are different from chemical reactions between small molecules. For example, polymers have structural features affecting their reactivities. More specifically, polymer chains may create a characteristic environment depending on their morphology. Such an environment includes functional groups, such as OH groups, on the polymer chains. In such a case reactants, such as tresylates, must diffuse through the environment before reaching the functional groups to be able to react with them. Therefore, it would be very difficult or almost impossible

for reactants added to the polymer to react with all of the functional groups on the polymer chains.

If the concentration of the polymer is so low that all of the polymer chains exist in a linear state, the reactant might approach the functional groups on the polymer chains. However, PVA disclosed in Tay is a cross-linked polymer which inherently possesses a polymeric network. Tay adds heparin to the cross-linked polymer. Therefore, it would be very difficult or almost impossible for tresylates to diffuse through the polymer network and react with all OH groups of the cross-linked PVA.

In contrast, the functionalized polymer of the present invention is a homopolymer represented by formula I, prepared by polymerizing monomers, each of which contains a glycosaminoglycan (GAG) portion such as heparin. Therefore, the invention does not suffer from the difficulties of Tay with regard to binding to each monomer, because in the invention heparin is not added to the polymer as it is in Tay.

In addition, Tay desires specific activity to a thrombin-antithrombin pair to achieve non-thrombosis (e.g., avoid bloodclotting). However, Table 1 indicates that the density of binding of heparin must be decreased to increase the specific activity; ("These results, given in Table 1, show the substantial decrease of specific activity as density of binding increases"). Therefore, Tay teaches away from maximizing heparins on PVA chains and does not disclose putting a heparin molecule on each monomer. In contrast, the inventive functionalized polymer has a maximum density of GAG's because the GAG's were introduced to the monomers before polymerization.

Larsson desires antithrombin activity. As taught by Tay, this requires decreasing heparin density on the polymer backbone. Therefore, Larsson does not disclose a heparin on each monomer.

The information in Larsson's own disclosure shows that heparin is not bound to every repeat unit. Larsson states that GAG residues should not be so close as to interfere with each other (col. 5, line 22, et seq.). Larsson discloses 500 heparins bound per molecule (col. 8, lines 22, et seq.) on polylysine, which has a molecular

weight >400,000. Using a lysine monomer molecular weight of 128 gives a heparin molecule per every 6.25 monomer units. Thus, Larsson fails to disclose heparin bound to each repeating unit.

In addition, Larsson adds heparin to the polymer (e.g., polylysine). Therefore, it is difficult or almost impossible to incorporate heparins to all amino groups of the polymer. Accordingly, Larsson fails to disclose the features of the claimed invention.

3. Claim 12 was rejected under 35 U.S.C. §102(b) in view of Joh (U.S. Patent 4,415,490). Claim 12 depends from claim 1 and thus includes all of its features. It is not proper to combine references in a §102 rejection. Therefore, it is assumed the rejection is based on Joh alone.

Joh discloses that heparin is bonded to an "aldehyde containing polymer." In Joh, heparin is bonded to the polymer via acetal or hemiacetal bonds (col. 7, top of the page). As can be seen from col. 6, line 60 through col. 7, line 8, Joh adds heparin to the formed polymer. Therefore, it would be difficult or almost impossible for heparin to diffuse through the polymer network and access every aldehyde, acetal or hemiacetal reactive site of the polymer chain. Accordingly, Joh does not disclose a carbohydrate group W bonded to each monomer of the polymer chain, as claimed.

It is respectfully submitted that the foregoing remarks place all pending claims in condition for allowance. Accordingly, an early Notice of Allowance for this application is respectfully requested.

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Respectfully submitted,

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